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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,989	03/03/2004	Adi Shefer	4686-121.2 US	4876

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EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1633	

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05/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/791,989	SHEFER ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above claim(s) *17-23 and 45-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 24-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, and further the following species: (A) as the pH sensitive material, Applicants elected acrylic acid or acrylic ester copolymer from claim 7; (B) as the water soluble material, Applicants elected polysaccharide from claim 10; (C) in regards to the requirement to elect one component of the nano-sphere which may be either a wax material or one fat material, Applicants elected candelilla wax from claim 16; in the reply filed on 10/25/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. In the reply filed 2/13/2008 Applicants stated that claims 6-7, 10, 12, 16 and 24 read on the elected species set forth above, and that claims 1-5, 8-9, 11, 13-15, and 25-44 read on the claims generically.

3. Claims 17-23 and 45-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/13/2008.

4. Therefore, claims 1-16 and 24-44 are presently pending for examination.

Specification

5. The use of the trademark EUDRAGIT® has been noted in this application, see for example line 23 of page 25. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-16, and 24-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urquhart et al. US 4,851,231 ('231), of record in view of US 5,718,919 to Ruddy and Roy et al. US 6,475,995.

Urquhart et al. discloses a pharmaceutical delivery system comprising a plurality of nanospheres encapsulated in a pH sensitive microsphere (drawings and descriptions thereof). The microsphere is a made from a polymer matrix which keeps its physical

and chemical integrity in a biological environment with a pH from 1.0 to 3.5, inclusive, and which degrades or dissolves to release the drug-laden nanospheres at a pH of 3.5 to 8.0 (col. 4, lines 9 – 29). Representative polymers include methymethacrylate-methacrylic acid copolymer (which qualifies as one of the poly(methyl methacrylates), as recited in claim 27, as an acrylic acid copolymer as recited in claim 7, and as a ligand, since any acid is a ligand for metals, as recited in claim 28), cellulose carboxylic acid esters (which is also a starch derivative, as recited in claim 24). The wall of the nanospheres in one embodiment comprises a wax, such as beeswax (col. 6, lines 38 – 54). With regard to claims 13 – 14, beeswax is deemed to inherently posses the properties required in these claims. The nanospheres are laden with drugs, specific examples of which are disclosed, and the disclosed drugs meet the requirements of instant claims requiring specific types of active agents (col. 7, line 53 – col. 8 line 32). With regard to claims 32-33, the nanospheres are taught to have a diameter of about 100 microns. The polymers included in the composition are all anionic, cationic, zwitterionic, or non-ionic, and all may be called "surface active agents" as required by claim 31. The release profile recited in claims 34-36 is deemed to be inherent, since the composition is the same, unless proven otherwise. The amount of the drug in the delivery system is disclosed (col. 8, lines 33 – 46), and this is deemed to be an amount sufficient to release the agent, as required by claims 34-36, since the device is designed to release the agent. From the figures, it is clear that tablets and capsules are disclosed embodiments of the invention. Capsules and tablets are articles, as recited in claim 42.

Furthermore, with regard to claims that require a second active agent, these claims do not require that the second active agent be different from the first.

What is lacking is the size of instant formulations and wherein the active agent is a nucleic acid. The formulations in the 231 reference are too large.

Ruddy teaches that it is advantageous to formulate drugs such as analgesics as nanoparticles in order to better control the anti-inflammatory action thereof.

Roy et al. describe nanoparticles used as a non-viral means for the delivery of nucleic acids in vivo. This non-viral delivery system is described as advantageous over viral systems to the extent that they can be designed for cell/tissue targeting and for producing a low immune response in comparison to viral systems.

It would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to make the formulation of '231 smaller, namely, to use nanoparticles encapsulated in a microparticle instead of microparticles encapsulated in a millimeter sized particle. The motivation comes from Ruddy, who teaches advantages of smaller sizes in drug delivery. Following the teachings of the references, the artisan would decrease the size of the millimeter sized particles of '231 proportionately with the size decrease in the microparticles, thus resulting in the instantly claimed invention. Additionally, one of ordinary skill in the art would have been motivated to modify the delivery system of Urquhart et al. to comprise a nucleic acid based drug since Roy et al. clearly teaches the benefits of using a non-viral nanoparticulate formulation over a viral delivery system in vivo.

9. Claims 40-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,851,231 ('231), of record, in combination with Roy et al., Ruddy and Gref et al, US 5,543,158.

The teachings of Urquhart et al., Roy et al. and Ruddy are discussed above.

10. '231 does not teach a method of administering the drug delivery system, nor does '231 teach a method of delivering the drug to all of the specific body parts mentioned in instant claims, although it does mention delivering medicine to the intestine. Gref teaches nanospheres for drug delivery that have PEG chains dangling from the exterior. Gref teaches that these PEG chains can be attached to antibodies in order to target specific cells or organs in the body (abstract, drawings, and descriptions thereof).

Thus, it would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to use attach antibodies to the nanospheres of '231 according to Gref. The motivation to do so is provided by Gref, who teaches that this manipulation allows for targeting to specific cells or organs. Since Gref teaches how to do this, the artisan would have a reasonable expectation of success. The expected result would be the drug delivery system of '231 with antibodies appended thereto according to Gref, wherein the system was able to target specific cells or organs, and thus be delivered to a specific part of the body.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-16 and 24-44 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 and 25-51 of copending Application No. 10/315,801. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of each application are drawn to a composition comprising a plurality of nanospheres encapsulated in a pH sensitive or salt-sensitive microsphere, the only difference is that the claims of the instant application are all limited to wherein the first active agent is a nucleic acid. It would have been obvious to the ordinary skilled artisan to modify the claims of the copending application to read on the claims of the instant invention since claim 32 of the copending application expressly recites wherein the active agent includes an oligonucleotide, which is a nucleic acid. Therefore, the claims of the instant application represent an obvious variation of the claims recited in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner, Art Unit 1633

/JLE/